REMARKS

Applicant thanks Examiner Wells for the courtesies extended to the undersigned in the telephone interview of August 28, 2003. Claims 1-4, 7-12, and 14-23 remain in this application. In this supplemental response, claims 1, 7, and 23 have been amended.

Applicant respectfully submits that no new matter has been added by this amendment. Support in the specification can be found at least on the following pages:

Support for amended claim 1 can be found at least on page 5, lines 9-18; and page 8, lines 17-39.

Support for amended claim 7 can be found at least on page 8, lines 17-39.

Support for amended claim 23 can be found at least on page 5, lines 9-18; page 6, lines 29-31; and page 8, lines 17-39.

Commentary on Interview of August 23, 2003

Applicant provides the following commentary on the interview of August 28, 2003.

The present invention provides stable compositions comprising a therapeutically effective amount of delta-9-tetrahydrocannabinol in a semiaqueous solvent for rapid aerosol delivery. (Specification at page 2, lines 34-35 to page 3, lines 1-12.) Delta-9-tetrahydrocannabinol is virtually insoluble in water (0.003 g/mL) and extremely lipophilic (oil/water coefficient of 9,400,000). (*Id.* at page 4, lines 16-23.) The lipophilic nature of delta-9-tetrahydrocannabinol suggests that formulations made primarily of lipophilic excipients such as oils, e.g., with sesame seed oil as currently approved for oral unit dosage use, would not be desirable for the present invention, which should be suitable for rapid bronchial delivery to the lung of a subject. (*Id.* at page 4, lines 28-33.)

Rapid bronchial delivery requires that the delta-9-tetrahydrocannabinol of the composition be near its solubility point and readily partition out of the formulation once released into the lung, so as to cross cell membranes rapidly and traverse the alveolar epithelial cells, interstitium, and endothelium to reach the blood stream. (*Id.* at page 4, lines 26-28 and page 5, lines 12-18.) However, in a formulation made with lipophilic excipients such as phospholipids, delta-9-tetrahydrocannabinol would have a stronger affinity for the formulation and partition out slowly, resulting in slower release of the drug from the formulation. (*Id.* at page 4, lines 34-35 to page 5, lines 1-3.)

Consequently, phospholipid excipients would materially affect the compositions of the present invention by altering the solubility of delta-9-tetrahydrocannabinol. (*Id.* at page 5, lines 32-35 to page 6, lines 1-3.) Increased solubility of delta-9-tetrahydrocannabinol in the formulation would likely decrease the *in vivo* bioavailability of delta-9-tetrahydrocannabinol. (*Id.* at page 5, lines 32-35 to page 6, lines 1-3; and page 11, lines 3-6.) In addition, a formulation containing phospholipids may not be aerosolized as easily as a formulation based on semiaqueous solvents as is the present invention. (*Id.* at page 5, lines 18-21.)

CONCLUSION

With entry of the above Amendment and in view of the foregoing Remarks, Applicant respectfully submits that the outstanding rejections and objections have been overcome, and that claims 1-4, 7-12, and 14-23 are in condition for allowance. Applicant respectfully requests withdrawal of the rejections and allowance of the claims.

None of Applicant's amendments are to be construed as dedicating any such subject matter to the public, and Applicant reserves all rights to pursue any such subject matter in this or a related patent application. If, in the opinion of the Examiner, a phone call may help to expedite

prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (312) 701-8775.

Respectfully submitted,

Dated: September 5, 2003 By: _____

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